

Amendments to the Specification:

Please replace the paragraph beginning on page 4, line 29, and ending on page 5, line 2, with the following amended paragraph:

In eukaryotes, the transcription elongation factor TFIIS, otherwise known as SII (Reines et al., J. Biol. Chem., 264: 10799-10809 (1989); Sluder et al., J. Biol. Chem., 264: 8963-8969 (1989)), is similar to the GreA and GreB proteins in that it stimulates RNA cleavage from the 3' end of RNA in a stalled complex but does not share significant sequence homology with the GreA and GreB proteins (Borukhov et al., Cell, *supra*). TFIIS stimulates either small- or large-fragment cleavage, depending on reaction conditions and the particular complex examined (Izban and Luse, J. Biol. Chem., 268: 12874-12885 (1993), *supra*; Wang and Hawley, *supra*). Evidence for functional similarity between prokaryotic and eukaryotic transcription elongation and read-through mechanisms has been found (Mote and Reines, J. Biol. Chem., 273: 16843-16852 (1998)).

Please replace the paragraph on page 11, lines 11-19, with the following amended paragraph:

Preferred mammalian polypeptides include t-PA, gp120, anti-HER-2, anti-CD20, anti-CD11a, anti-CD18, anti-CD40, DNase, IGF-I, IGF-II, FGF-5, thrombopoietin, brain IGF-I, ~~thrombopoietin~~, growth hormone, relaxin chains, growth hormone releasing factor, insulin chains or pro-insulin, urokinase, immunotoxins, neurotrophins, and antigens. Particularly preferred mammalian polypeptides include, e.g., t-PA, gp120(IIb), anti-HER-2, anti-CD20, anti-CD11a, anti-CD18, anti-CD40, DNase, thrombopoietin, IGF-I, IGF-II, FGF-5, growth hormone, NGF, NT-3, NT-4, NT-5, and NT-6, and most preferably, FGF-5 and thrombopoietin.

Please replace the paragraph on page 19, lines 8-29, with the following amended paragraph:

E. coli strain W3110 is a preferred host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell should secrete minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in

the genes encoding proteins, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonAΔ* (also known as *ΔfhuA*); *E. coli* W3110 strain 9E4, which has the complete genotype *tonAΔ ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonAΔ ptr3 phoAΔE15 Δ(argF-lac)169 ompTΔ degP41kan^r*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonAΔ ptr3 phoAΔE15 Δ(argF-lac)169 ompTΔ degP41kan^r rbs7Δ ilvG*; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin-resistant *degP* deletion mutation; *E. coli* W3110 strain 33D3, which has the complete genotype *tonA ptr3 lacIq LacL8 ompT degP kan^r*; *E. coli* W3110 strain 36F8, which has the complete genotype *tonA phoA Δ(argF-lac) ptr3 degP kan^r ilvG+*, and is temperature resistant at 37°C; an *E. coli* strain having the mutant periplasmic protease(s) disclosed in U.S. Pat. No. 4,946,783 issued August 7, 1990; *E. coli* W3110 strain 52A7, which has the complete genotype *tonAΔ (fhuAΔ) lonΔ gale rpoHts (htpRts) ΔclpP lacIq*; *E. coli* W3110 strain 54C2, which has the complete genotype *fhuA(tonA)lon gale rpoHts(htpRts) clpP lacIq*; and *E. coli* W3110 strain 59B9, which has the complete genotype *fhuAΔ(tonAΔ)lonΔ gale rpoHts(htpRts) ΔclpP lacIq ΔompT Δ(nmpc-fepE) ΔlacY*.

Please replace the paragraph on page 21, lines 18-24, with the following amended paragraph:

For secretion of an expressed or over-expressed gene product, the host cell is cultured under conditions sufficient for secretion of the gene product. Such conditions include, e.g., temperature, nutrient, and cell-density conditions that permit secretion by the cell. Moreover, such conditions are those under which the cell can perform basic cellular functions of transcription, translation, and passage of proteins from one cellular compartment to another, as are known to those skilled in the art.

Please replace the paragraph on page 22, lines 14-19, with the following amended paragraph:

The following procedures are exemplary of suitable purification procedures: fractionation on immunoaffinity or ion-exchange columns; ethanol precipitation; reverse-phase HPLC; chromatography on silica or

on ~~a cation-~~ an anion-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium-sulfate precipitation; and gel filtration using, for example, SEPHADEX™ G-75 medium from Amersham Biosciences.

Please replace the paragraph on page 23, lines 27-36, with the following amended paragraph:

Three DNA fragments were ligated together to make pMP331 as shown in Figure 1, the first of which was the large fragment of the vector pdh108 previously cut with XbaI and StuI. pdh108 is derived from the vector pHG207-1 (DeBoer et al., Promoters: Structure and Function (Praeger: New York, 1982), pp. 462-481) and contains the λ transcriptional terminator downstream of the *trp* promoter. The second part was the 431-base-pair XbaI-BamHI fragment from the plasmid pMP202 encoding the first 122 amino acids of TPO. The third part was an approximately 669-base-pair BamHI-RsaI fragment from phmp11 (deSavauge et al., Nature, 369: 533-538 (1994)) encoding the last half of the TPO gene product.

Please replace the paragraph beginning on page 25, line 34, and ending on page 26, line 2, with the following amended paragraph:

Plasmid pMP1016

The plasmid pMP1016 is a derivative of pMP331 in which the *trp* promoter has been replaced with the AP promoter. This plasmid was constructed as shown in Figure 8 by ligating together two DNA fragments. The first of these was the vector pST182 in which the small XbaI-SphI fragment had been removed. The plasmid pST182 is a derivative of phGH1 (Chang et al., Gene, 55: 189-196 (1987)), and this latter vector could be used instead to generate this DNA fragment. The second part in the ligation was a 1791-base-pair XbaI-SphI fragment from pMP331 encoding the TPO gene product and the λ transcriptional terminator.

Please replace the paragraph on page 36, lines 10-17, with the following amended paragraph:

Quantitation of 10Sa-tagged and full-length TPO

Samples from the shake-flask cultures described above were prepared and run on SDS-PAGE, transferred to nitrocellulose, and probed

with a polyclonal antibody raised against either TPO₁₅₃ or the 10Sa peptide. The blots were then scanned using an optically enhanced laser densitometer (PDI, Inc., model 325oe). The peak areas for the full-length TPO, as well as the other TPO species that cross-react with the TPO₁₅₃ polyclonal antibody, were determined.

Please replace the paragraph on page 36, lines 18-21, with the following amended paragraph:

The same set of shake-flask samples was also run on SDS-PAGE and stained with Coomassie Blue. The gels were scanned using an optically enhanced laser densitometer (PDI, Inc., model 325oe) and the percentage of total cell protein represented as full-length TPO was calculated.

Please replace the paragraph on page 39, lines 19-23, with the following amended paragraph:

Culture of transformed cells

The transformed cells were grown up in a fermentor under conditions described in Example 2 for the *trp* plasmids pMP331 and pMP951, except that the IPTG solution was used only for pFGF5IT-AT and not for pFGF5IT. Whole-cell lysates from the fermentation samples were prepared for SDS-PAGE.

Please replace the paragraph on page 40, lines 10-18, with the following amended paragraph:

Materials and Methods:

Shake-flask experiments with FGF-5 and GreA or GreB co-expression:

The strain 59B9 {W3110 *fhuAA(tonAA) lonΔ gale rpoHts(htpRts) ΔclpP lacIq ΔompT Δ(nmpc-fepE) ΔlacY*} was transformed with pFGF5IT-PhoA (described in Example 4) or pFGF5IT-PhoAAT, either alone or in combination with pDR1 or pDR3, each of which is described above. The plasmid pFGF5IT-PhoAAT is a derivative of pFGF5IT in which the same anti-termination element is present as in pFGF5IT-AT described in Example 4, and in which the *trp* promoter is replaced by the AP promoter (Kikuchi et al., *supra*).

Please replace the paragraph on page 40, lines 29-35, with the following amended paragraph:

Samples from the shake_flask cultures described above were prepared and run on SDS-PAGE, transferred to nitrocellulose, and probed with a polyclonal antibody raised against either FGF-5 (R&D Systems) or the 10Sa peptide. The blots were then scanned using an optically enhanced laser densitometer (PDI, Inc., model 325oe). The peak areas for the full-length FGF-5, as well as the other FGF-5 species that cross-react with the FGF-5 polyclonal antibody, were determined.